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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/595,891	05/18/2006	Dominique Jean-Pierre Mabire	PRD-2120USPCT	8597

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EXAMINER	
MCDOWELL, BRIAN E	

ART UNIT	PAPER NUMBER
1624	

MAIL DATE	DELIVERY MODE
12/31/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/595,891	MABIRE ET AL.	
	Examiner	Art Unit	
	BRIAN MCDOWELL	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *03 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

BEM

Detailed Action

DETAILED ACTION

Status of Claims

Claims 1-16 have been cancelled. Claims 17-22 are pending and are new claims.

Status of Claim Objections

Applicant's cancellation of claims 1-16, see Remarks, filed 11/3/2008, with respect to the Non-Final Office Action mailed 7/3/2008 has been noted, thus the objection is withdrawn.

Status of Rejections

35 USC § 112 (2nd Paragraph)

Applicant's cancellation of claims 1-16, see Remarks, filed 11/3/2008, with respect to the Non-Final Office Action mailed 7/3/2008 has been noted, thus the rejection is withdrawn.

35 USC § 103

Applicant's arguments and amendment of claims 1,2,7, and 13, see Remarks, filed 11/3/2008, with respect to the Non-Final Office Action mailed 7/3/2008 have been fully considered and are persuasive. The rejection has been withdrawn.

Double Patenting

Applicant's arguments of claims 1-4,7, and 13, see Remarks, filed 11/3/2008, with respect to the Non-Final Office Action mailed 7/3/2008 have been fully considered

but are not persuasive. The rejection may be removed once the appropriate terminal disclaimer or appropriate amendment of the claims that would render the copending claims nonobvious is filed.

New Objections and Rejections

Claim Rejections - 35 USC § 112 (2nd Paragraph)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 18-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 18 recites the limitation "-Z is a heterocyclic ring system selected from (c-1),(c-2),(c-4)". There is insufficient antecedent basis for this limitation in the claim (e.g., (c-2 and (c-4)).

Claims 18 and 19 are indefinite for containing a broad and a narrow limitation in the same claim. For example, in the instant claims, a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render

a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present claims 18-19, applicant states that R^3 is a group of formula (b-1), then recites limitations for said formula in the same claim, which is the narrower statement of the range/limitation.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 17-22 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4,6,12,14-16,

and 26-30 of copending Application No. 10/595882. Although the conflicting claims are not identical, the compounds within the instant application are so closely related in structure to those in application '882, it would render them obvious.

Both claims 17-22 in the instant application and claims 1-4,6,12,14-16,and 26-30 in '882 refer to 2-quinoxalinones and 2-quinolinones of the general formula I and/or simple compositions containing said compounds.

The difference from the instant claims and the claims in '882 in regards to the formula I is that the quinoxalinone/quinolinone core is substituted with the phenylalkyl substituent at the 6-position instead of the 7-position, respectively. The compounds are obvious variants (regioisomers) since MPEP 2144.09 states *"Compounds which are position isomers (compounds having the same radicals in physically different positions on the same nucleus) or homologs (compounds differing regularly by the successive addition of the same chemical group, e.g., by -CH2- groups) are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties. In re Wilder, 563 F.2d 457, 195 USPQ 426 (CCPA 1977).*

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 103

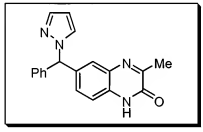
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

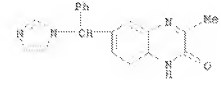
Claims 17,18, and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Venet *et al.* (US Patent 5,028,606).

Applicant may have a specie that reads on the aforementioned claims:



wherein R_1 = methyl, n = 0, X = N, R^2 = H, R^3 = pyrazolyl (c-3), and $R^{4\text{-}6,12}$ = H.

Venet teaches the following compound:



wherein R_1 = methyl, n = 0, X = N, R^2 = H, R^3 = imidazolyl, and $R^{4\text{-}6,12}$ = H (see col.43, compound 57 in table 9).

The only difference between applicant's compound and the compound described in the Venet document is the substituent R^3 (imidazolyl versus pyrazolyl). However, the two compounds are just regioisomers. MPEP 2144.09 states *"Compounds which are position isomers (compounds having the same radicals in physically different positions on the same nucleus are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties. In re Wilder, 563 F.2d 457, 195 USPQ 426 (CCPA 1977).*

In summary, applicant is taking a well-known compound that is described in the literature and doing a simple modification to the molecule (atom flipping on the heterocyclic ring). Therefore, a person of ordinary skill would have a reasonable expectation of success in obtaining a biologically active molecule.

Therefore, applicant's claims are obvious over the prior art.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 22 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Pursuant to In re Wands, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), one considers the following factors to determine whether undue experimentation is required:

(A) The breadth of the claims;

(B) The nature of the invention;

(C) The state of the prior art;

(D) The level of one of ordinary skill;

(E) The level of predictability in the art;

(F) The amount of direction provided by the inventor;

(G) The existence of working examples; and

(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Some experimentation is not fatal; the issue is whether the amount of experimentation is "undue"; see In re Vaeck, 20 USPQ2d 1438, 1444. Analysis is described below:

(A) Breadth of claims: The claims encompass thousands of compositions containing compounds of the present invention (2-quinoxalinones and 2-quinolinones) along with any chemotherapeutic agent. Thus, the scope of the claims is very broad.

(B) The nature of the invention: 2-quinoxalinones and 2-quinolinones as poly(ADP-ribose)polymerase-1 inhibitors.

(C) State of the Prior Art: Chemotherapeutic agents may encompass millions of compounds, each of which may have different modes of action for the treatment of various diseases. Some examples are the following:

an opioid analgesic, e.g. morphine, heroin, hydromorphone, oxymorphone, levorphanol, levallorphan, methadone, meperidine, fentanyl, cocaine, codeine, dihydrocodeine, oxycodone, hydrocodone, propoxyphene, nalmefene, nalorphine, naloxone, naltrexone, buprenorphine, butorphanol, nalbuphine or pentazocine;

a nonsteroidal antiinflammatory drug (NSAID), e.g. aspirin, diclofenac, diflunisal, etodolac, fenbufen, fenoprofen, flufenisal, flurbiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, meclofenamic acid, mefenamic acid, meloxicam, nabumetone, naproxen, nimesulide, nitroflurbiprofen, oxaprozin, piroxicam, phenylbutazone, piroxicam, sulfasalazine, sulindac, tolmetin or zomepirac;

a barbiturate sedative, e.g. amobarbital, aprobarbital, butalbarbital, butabital, mephobarbital, metharbital, methohexital, pentobarbital, phenobarbital, secobarbital, talbutal, thiamylal or thiopental;

a benzodiazepine having a sedative action, e.g. chlordiazepoxide, clorazepate, diazepam, flurazepam, lorazepam, oxazepam, temazepam or triazolam;

an H_1 antagonist having a sedative action, e.g. diphenhydramine, pyrilamine, promethazine, chlorpheniramine or chlorcyclizine;

a sedative such as glutethimide, meprobamate, methaqualone or dichloralphenazone;

a skeletal muscle relaxant, e.g. baclofen, carisoprodol, chlorzoxazone, cyclobenzaprine, methocarbamol or orphenadrine;

an NMDA receptor antagonist, e.g. dextromethorphan ((+)-3-hydroxy-N-methylmorphinan) or its metabolite dextrorphan ((+)-3-hydroxy-N-methylmorphinan), ketamine, memantine,

pyrroloquinoline quinine, cis-4-(phosphonomethyl)-2-piperidinecarboxylic acid, budipine, EN-3231 (MorphiDex®, a combination formulation of morphine and dextromethorphan), topiramate, memantine or perzinfotel including an NR2B antagonist, e.g. ifenprodil, traxoprodil or (+)-(R)-6-(2-[4-(3-fluorophenyl)-4-hydroxy-1-piperidinyl]-1-hydroxyethyl-3,4-dihydro-2(1H)-quinolinone;

an alpha-adrenergic, e.g. doxazosin, tamsulosin, ephedrine, guanfacine, dexmetatomidine, modafinil, or 4-amino-6,7-dimethoxy-2-(5-methane-sulfonamido-1,2,3,4-tetrahydroisoquinol-2-yl)-5-(2-pyridyl) quinazoline;

a tricyclic antidepressant, e.g. desipramine, imipramine, amitriptyline or nortriptyline;

an anticonvulsant, e.g. carbamazepine, lamotrigine, topiramate or vigabatrin;

This is only a fraction of compounds that may be considered "chemotherapeutic agents".

(D) Skill of those in the art: The level of skill in the art is high.

(E) Level of predictability in the art: It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(F) Direction or Guidance: Little guidance or direction is provided by applicant in regards to obtaining compositions that contain a "chemotherapeutic agent" along with the synthesized compounds of the present invention.

(G) Working Examples: There are no working examples provided by applicant in regards to compositions that contain a chemotherapeutic agent and compounds of the present invention. One of ordinary skill could not extrapolate how to make and/or use these compositions from applicant's disclosure.

(H) The quantity of experimentation needed: Since there are no working examples as described above, the amount of experimentation is expected to be high and burdensome. One skilled in the art could not take the information provided in the disclosure to make and use the claimed compositions. One of ordinary skill would not expect every possible chemotherapeutic agent in combination with the compounds of the present invention to work perfectly in a synergistic manner to afford potent therapeutic agents. Therefore undue experimentation would be expected.

Due to the level of unpredictability in the art, the very limited guidance provided, and the lack of working examples, the applicant has shown lack of enablement. MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BRIAN MCDOWELL whose telephone number is (571)270-5755. The examiner can normally be reached on Monday-Thursday 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached 571-272-0661. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BM

/James O. Wilson/

Supervisory Patent Examiner, Art Unit 1624